



ORAL PRESENTATION

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Role of Ras isoforms in $\gamma\delta$ T-cell development

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Introduction

The small guanine nucleotide binding proteins of the Ras family (H-, K-, and N-ras isoforms) couple surface receptors, including T-cell antigen receptors, to a variety of cellular responses. Ras proteins are highly homologous and expressed ubiquitously, raising questions as to their functional specificity. H-ras and N-ras have been shown to be dispensable for development in the thymus but critical for peripheral Th1 differentiation of $\alpha\beta$ T cells [1]. In the $\gamma\delta$ T-cell lineage, in contrast, the specific function of Ras isoforms had not been addressed.

Aim

We aimed at identifying the specific roles of H-ras and N-ras in $\gamma\delta$ T-cell development, particularly, in the generation of $\gamma\delta$ T-cell subsets defined by expression of CD27.

Mice and methods

Mice deficient for H-ras or N-ras were analyzed by multiparametric flow cytometry. In addition, N-ras-deficient mice with impaired $\alpha\beta$ T-cell development were generated by breeding with CD3 δ KO mice and analyzed.

Results

Ras isoform-deficient mice exhibited normal frequencies and numbers of $\gamma\delta$ T cells in the thymus, which expressed normal levels of surface $\gamma\delta$ TCR, but a consistent decrease of CD27⁺ $\gamma\delta$ T cells in peripheral lymphoid organs, compared to controls. Conversely, in mice lacking mature $\alpha\beta$ T cells, N-ras deficiency resulted in reduced numbers of CD27⁺ $\gamma\delta$ T cells, with concomitant increase of the CD27⁻ population, in the thymus but not in the periphery. This suggests that signals from $\alpha\beta$ T-cell thymocytes for developing CD27⁺ $\gamma\delta$ T cells are partly N-ras-dependent.

Conclusions

As previously shown for $\alpha\beta$ T cells, H-ras and N-ras are dispensable for intrathymic development of $\gamma\delta$ T cells, but they could be involved in finely regulating survival and/or expansion of $\gamma\delta$ T cells in the periphery, in agreement with recent findings in mice lacking RasGRP1 [2], a guanine nucleotide exchange factor for Ras.

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